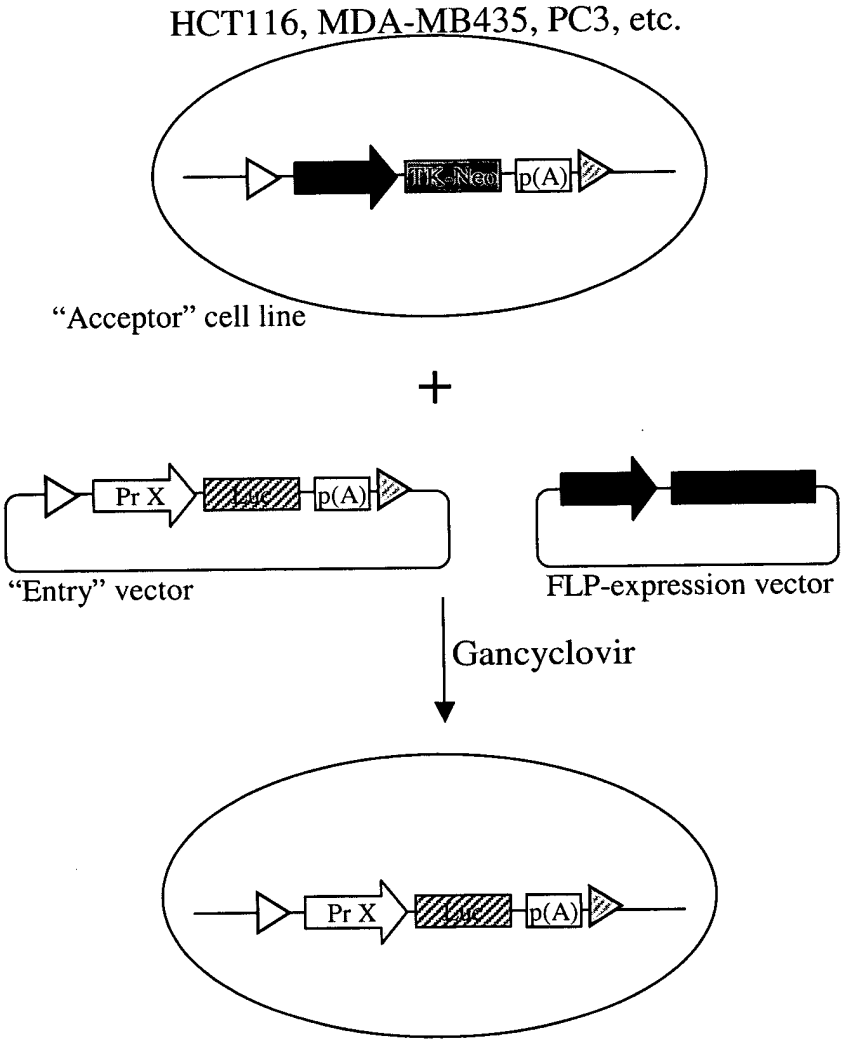

HCT116, MDA-MB435, PC3, etc.
TK-Neo
p(A)
"Acceptor" cell line
+
Pr X
Luc
p(A)
"Entry" vector
FLP-expression vector
Gancyclovir
Pr X
Luc
p(A)

Figure 1

Figure 2A

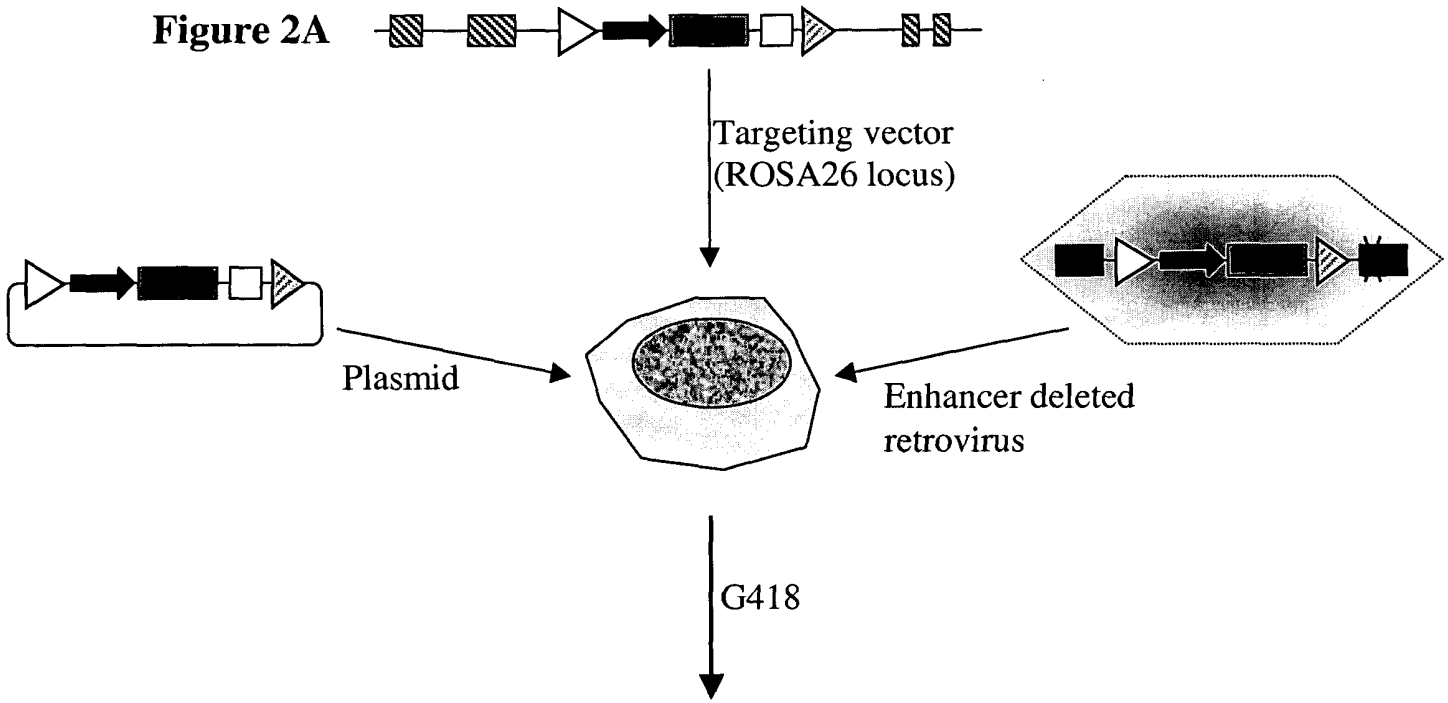
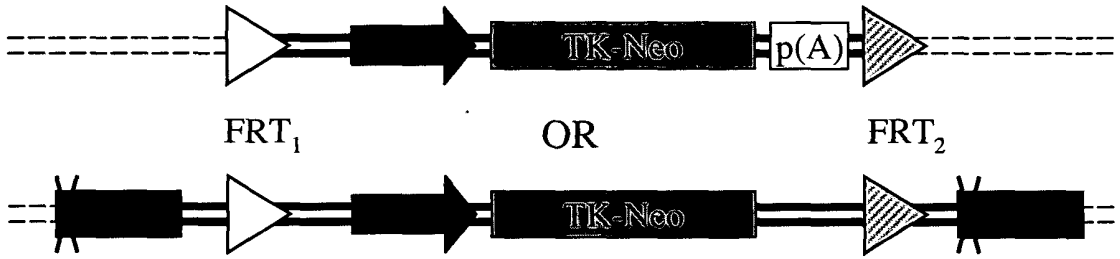
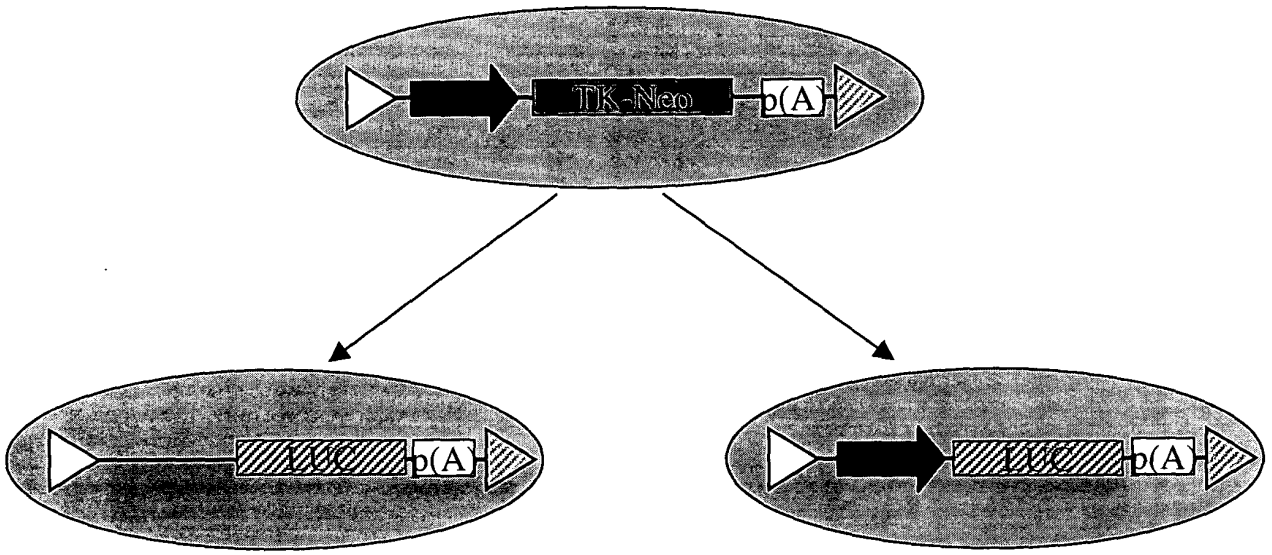


Figure 2B





	Promoterless Luc Activity	CMV Promoter Luc Activity	Integration Site Interpretation
	High	High	Nearby strong promoter
	Low	Low	Nearby silencing element
→	Low	High	"Neutral" site

Figure 3

Figure 4A

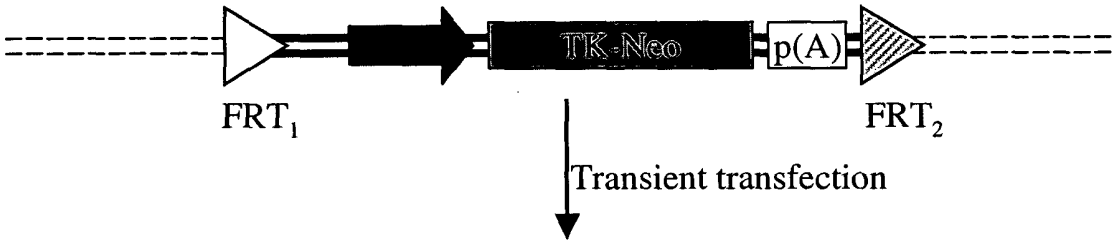


Figure 4B

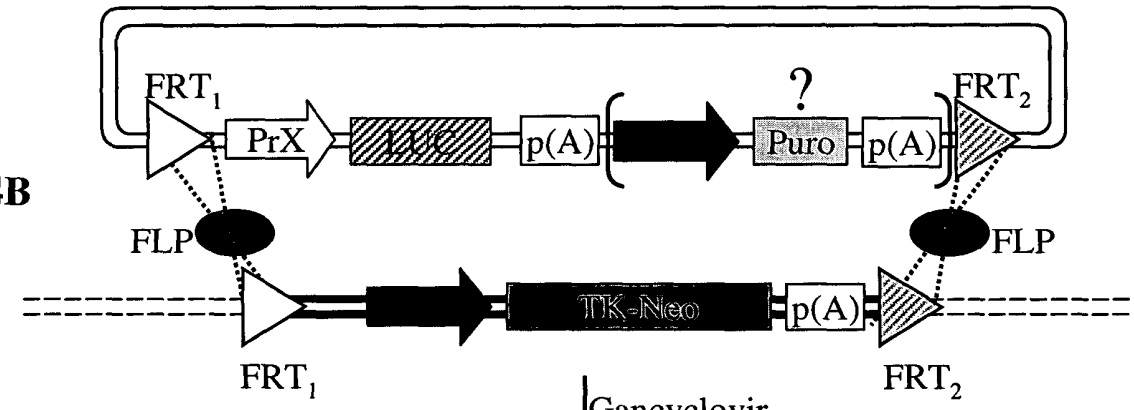
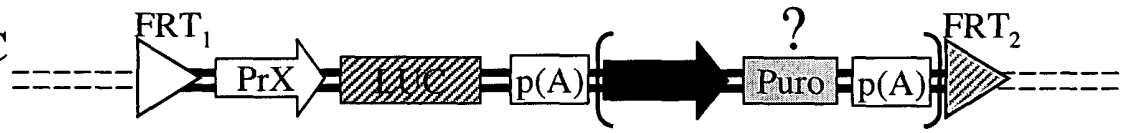


Figure 4C



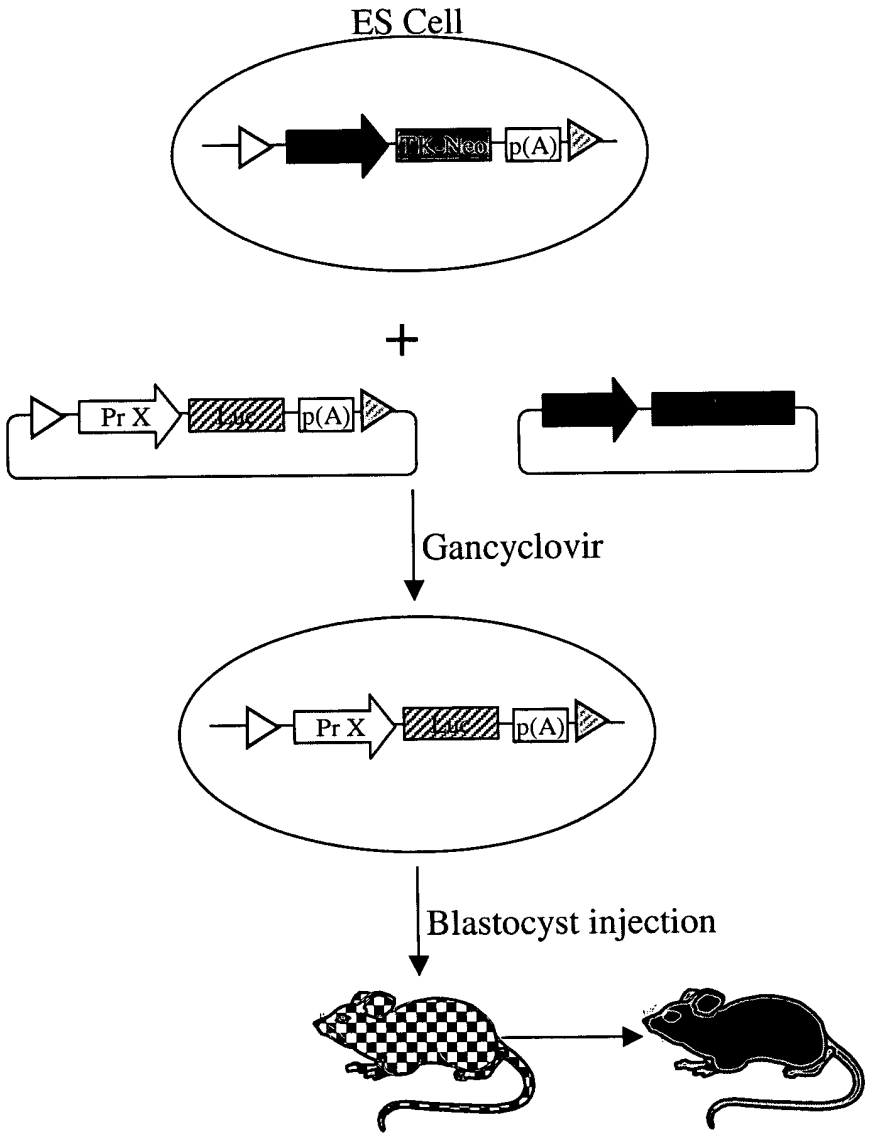

ES Cell
TK-Neo
p(A)
+
Pr X
Luc
p(A)
Gancyclovir
Pr X
Luc
p(A)
Blastocyst injection

Figure 5

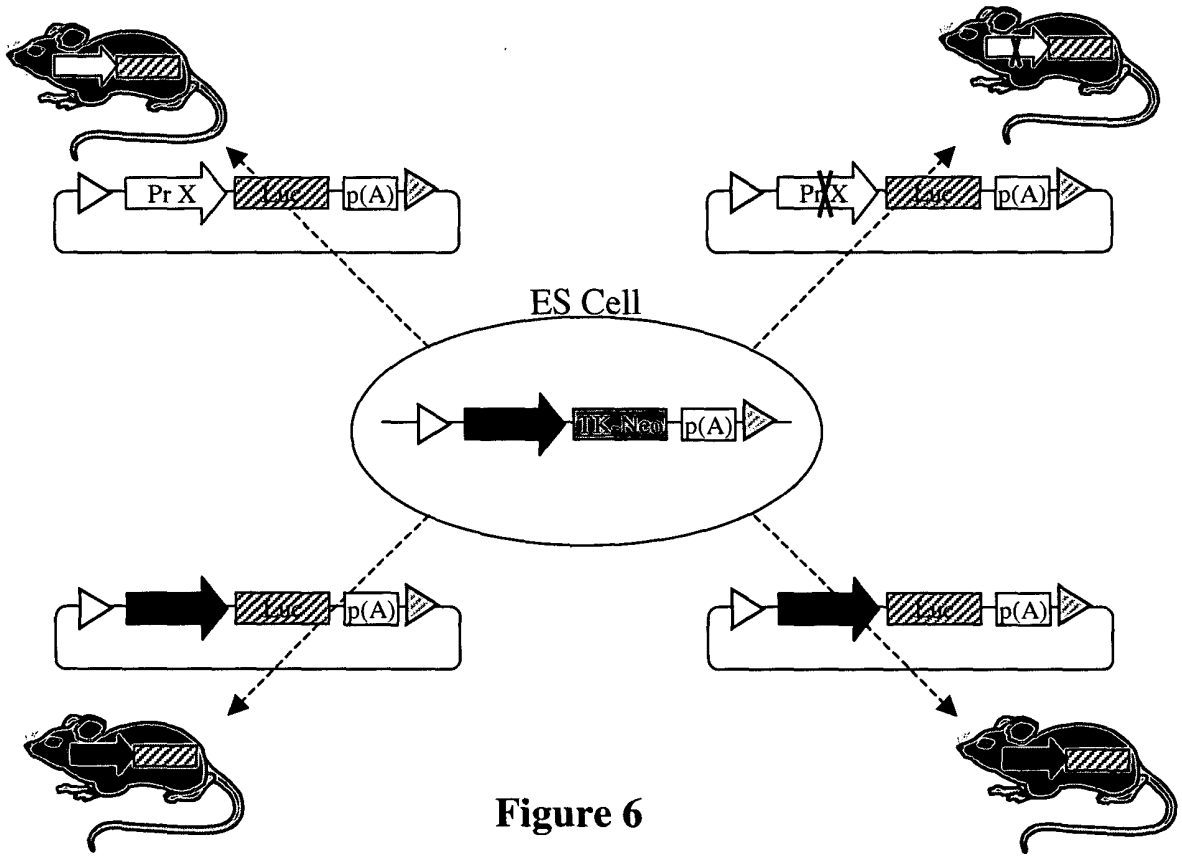


Figure 6

Figure 7A

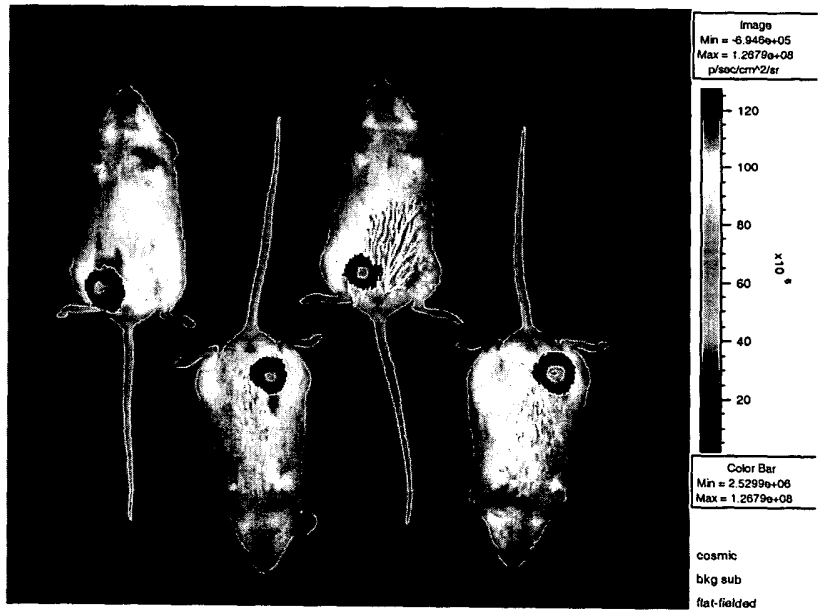


Figure 7B

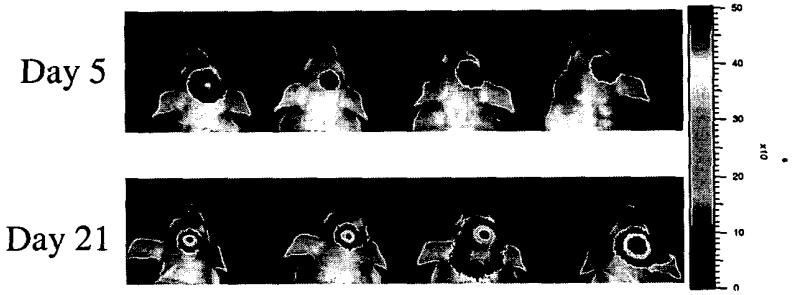


Figure 8 - Orthotopic brain tumor model.
Nude mice were implanted with 50,000 U87-Luc cells. Mice were anesthetized and imaged 5 and 21 days after implantation. Absolute photonic flux over a 2 minute imaging interval is indicated by the false color scale.

Figure 9A

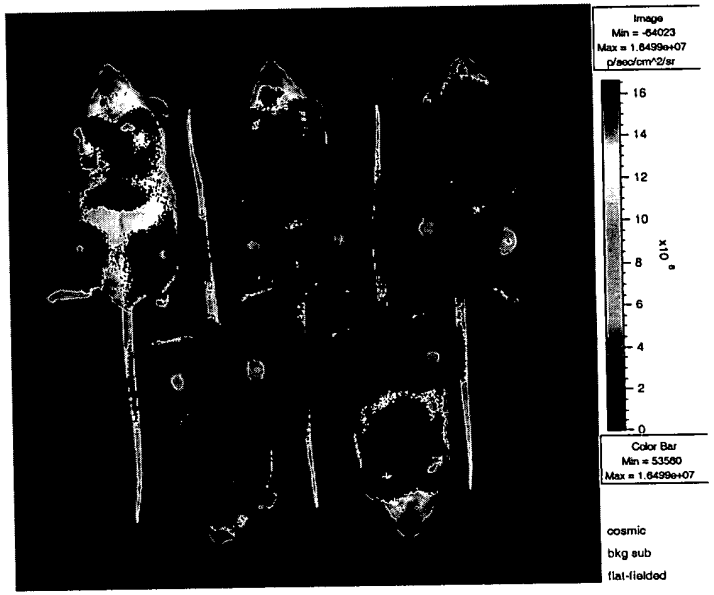
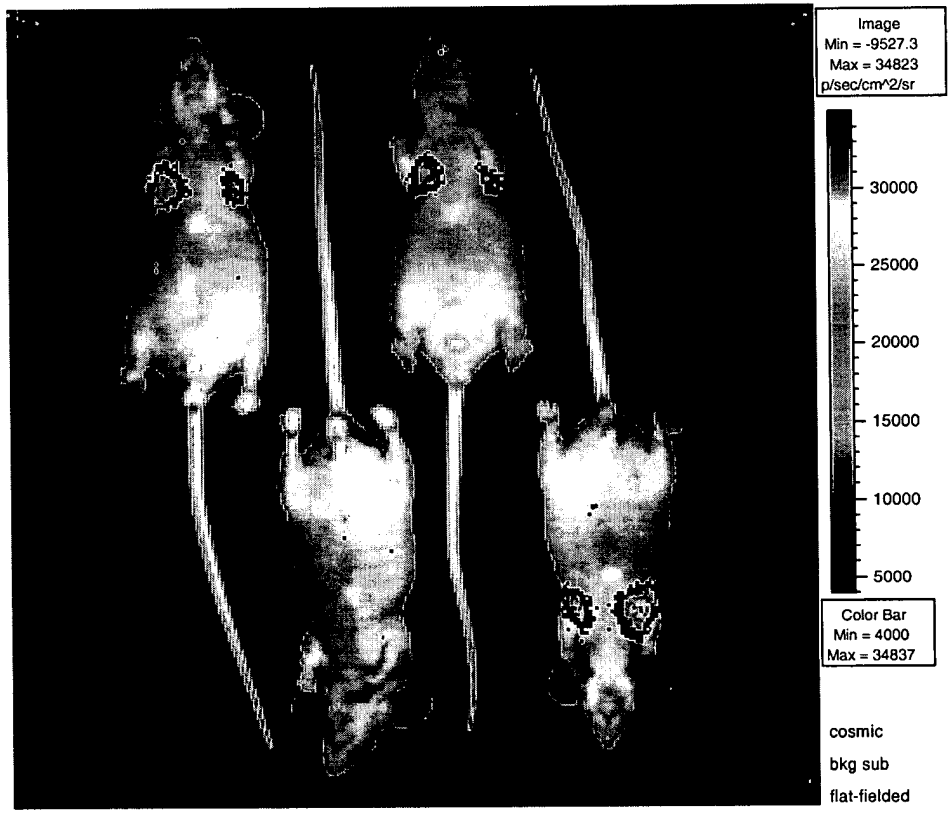


Figure 9B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Max = 34823
p/sec/cm^2/sr
30000
25000
20000
15000
10000
5000
Color Bar
Min = 4000
Max = 34837
cosmic
bkg sub
flat-fielded

Figure 10

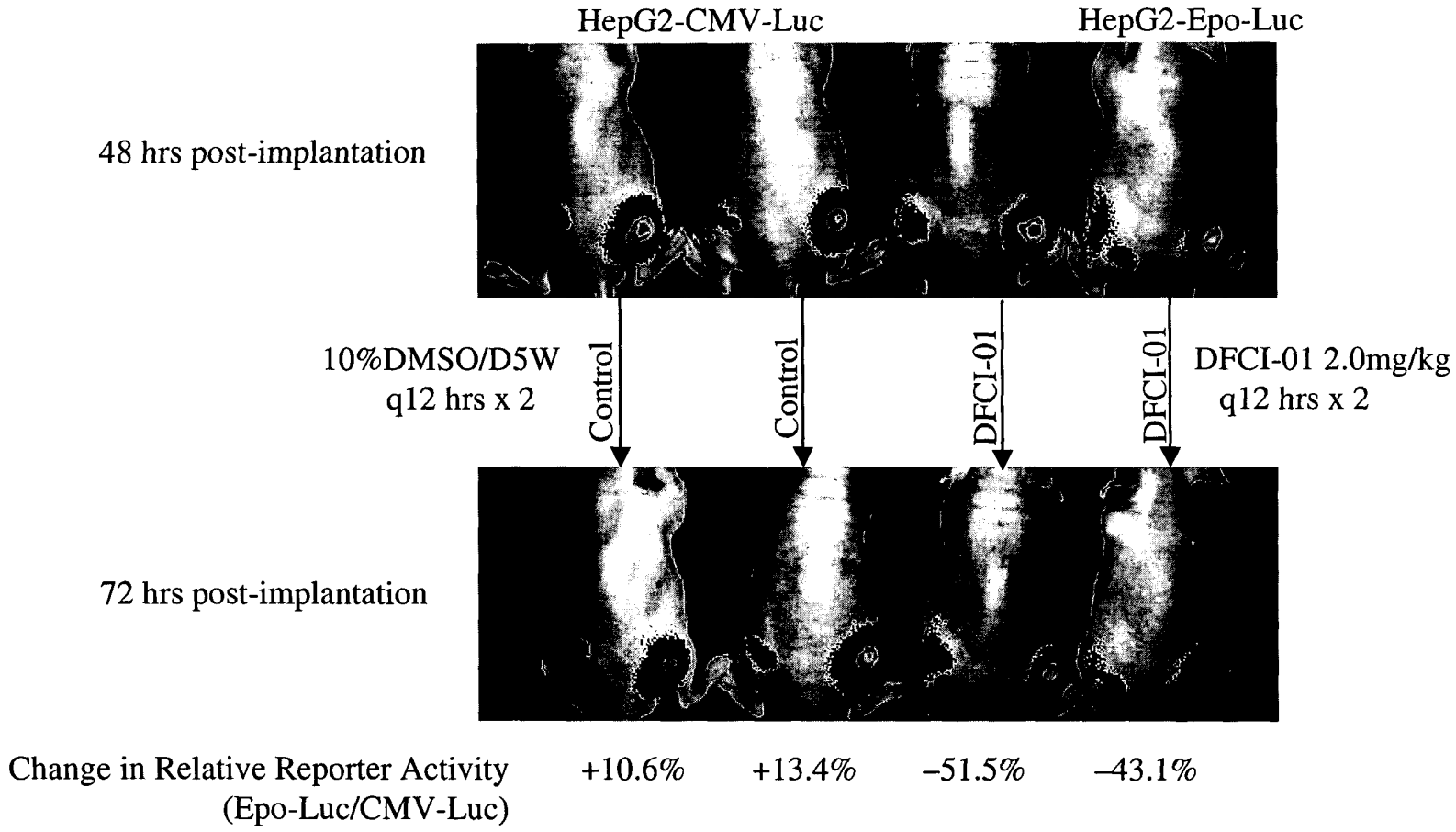

HepG2-CMV-Luc
HepG2-Epo-Luc
48 hrs post-implantation
10%DMSO/D5W
q12 hrs x 2
Control
Control
DFCI-01
DFCI-01
DFCI-01 2.0mg/kg
q12 hrs x 2
72 hrs post-implantation
Change in Relative Reporter Activity
(Epo-Luc/CMV-Luc)
+10.6%
+13.4%
–51.5%
–43.1%

Figure 11

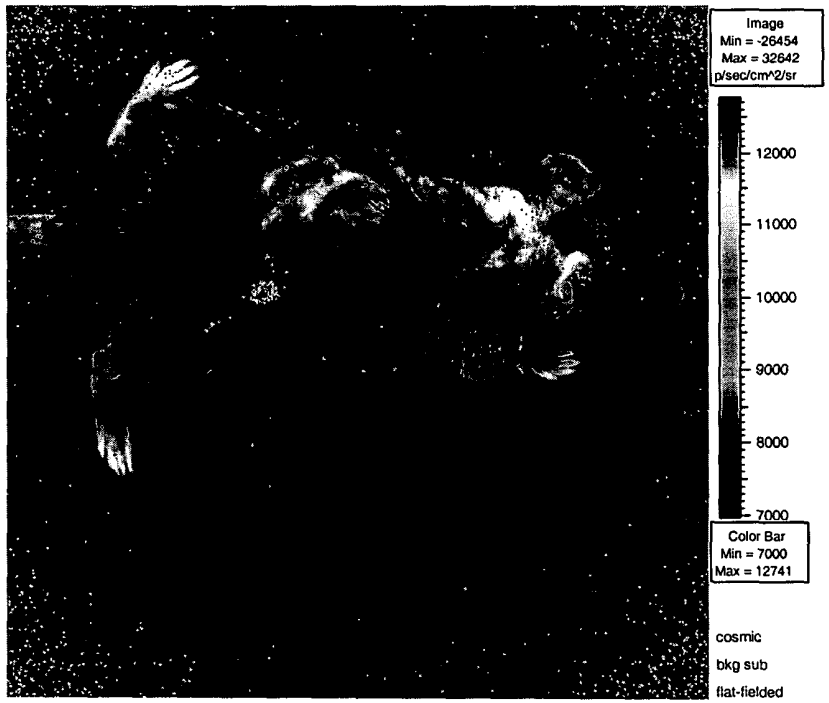


Image
Min = -26454
Max = 32642
p/sec/cm^2/sr
12000
11000
10000
9000
8000
7000
Color Bar
Min = 7000
Max = 12741
cosmic
bkg sub
flat-fielded

Figure 12

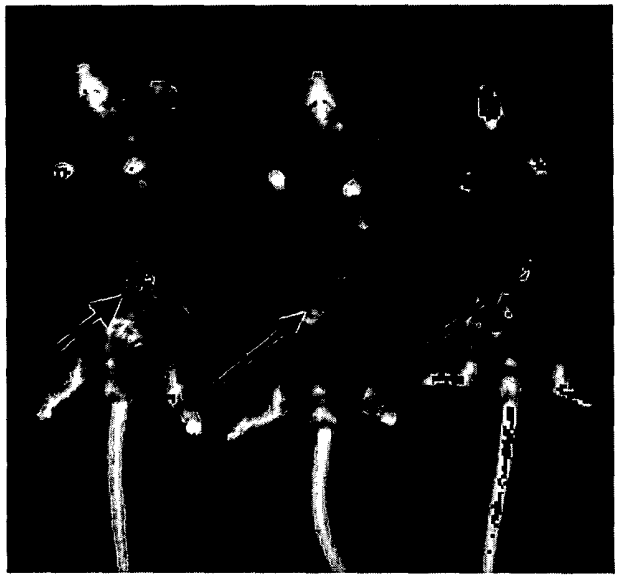


Figure 13.
3 mice carrying the Ang2-Luc transgene were injected with Matrigel with VEGF and bFGF (arrows). Mice were imaged 72 hrs after injection. Mice 1 and 3 show specific emission from sites of VEGF/bFGF implantation, and are potentially angiogenesis-specific reporter mice.

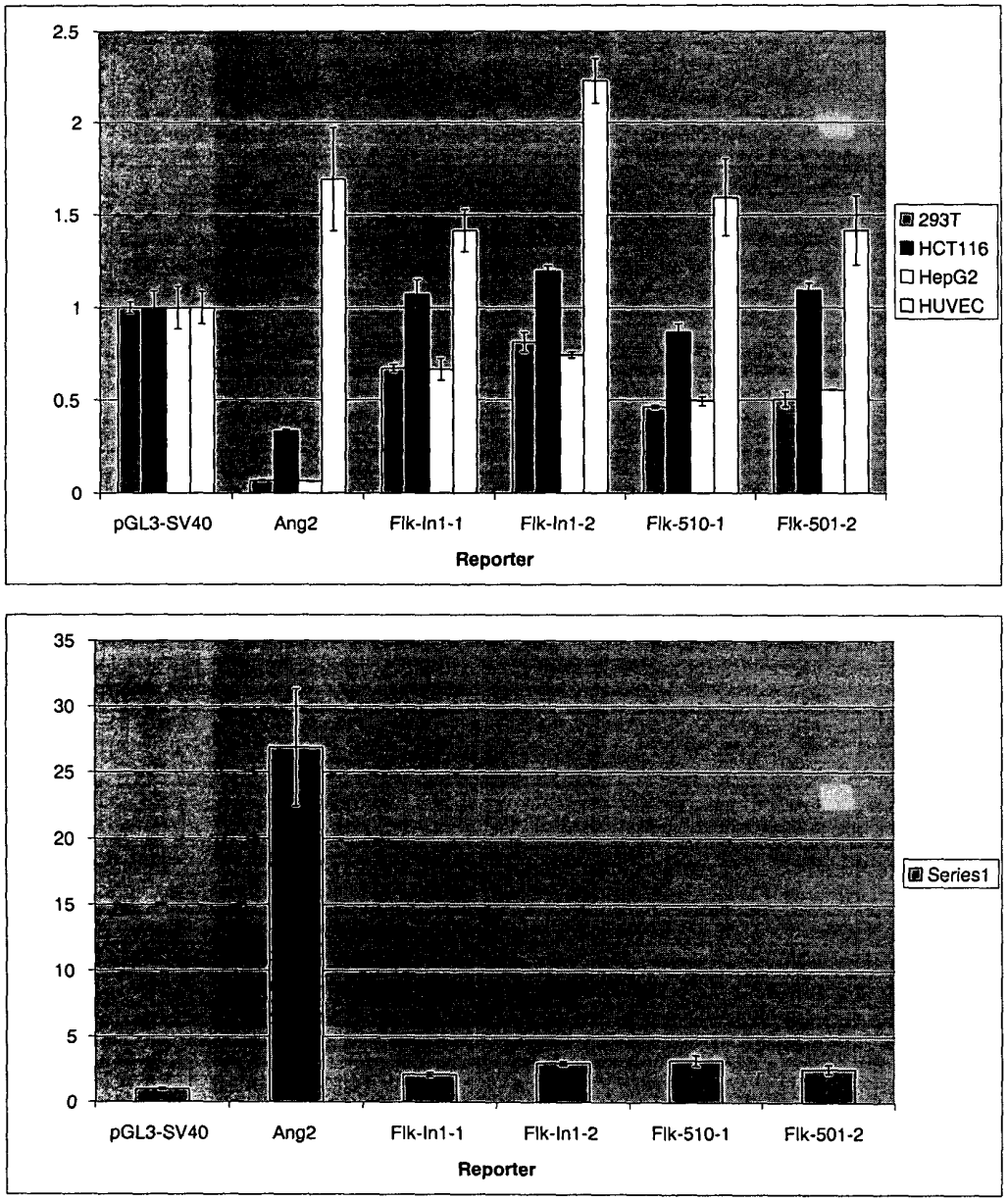


Figure 14.
Specificity of Ang2 promoter. The Ang2 promoter sequence was determined by search of the mouse genome database. Approximately 1kb of sequence preceding the coding sequence was amplified by PCR and cloned before the luciferase gene. This reporter was transfected into the indicated cell lines (293T, HCT116, HepG2) and into human umbilical vein endothelial cells (HUVEC). For comparison, a SV40 promoter driven luciferase was used. Also, the various Flk constructs are endothelial-specific reporters, described previously. As a measure of specificity, the activity in endothelial cells relative to HepG2 cells (hepatoma) shows the Ang2 promoter is much more specific in comparison to Flk reporters (lower panel).

MLL Leukemia Cell Line TS(4;11) Treated with FLT3 Inhibitor PKC-412

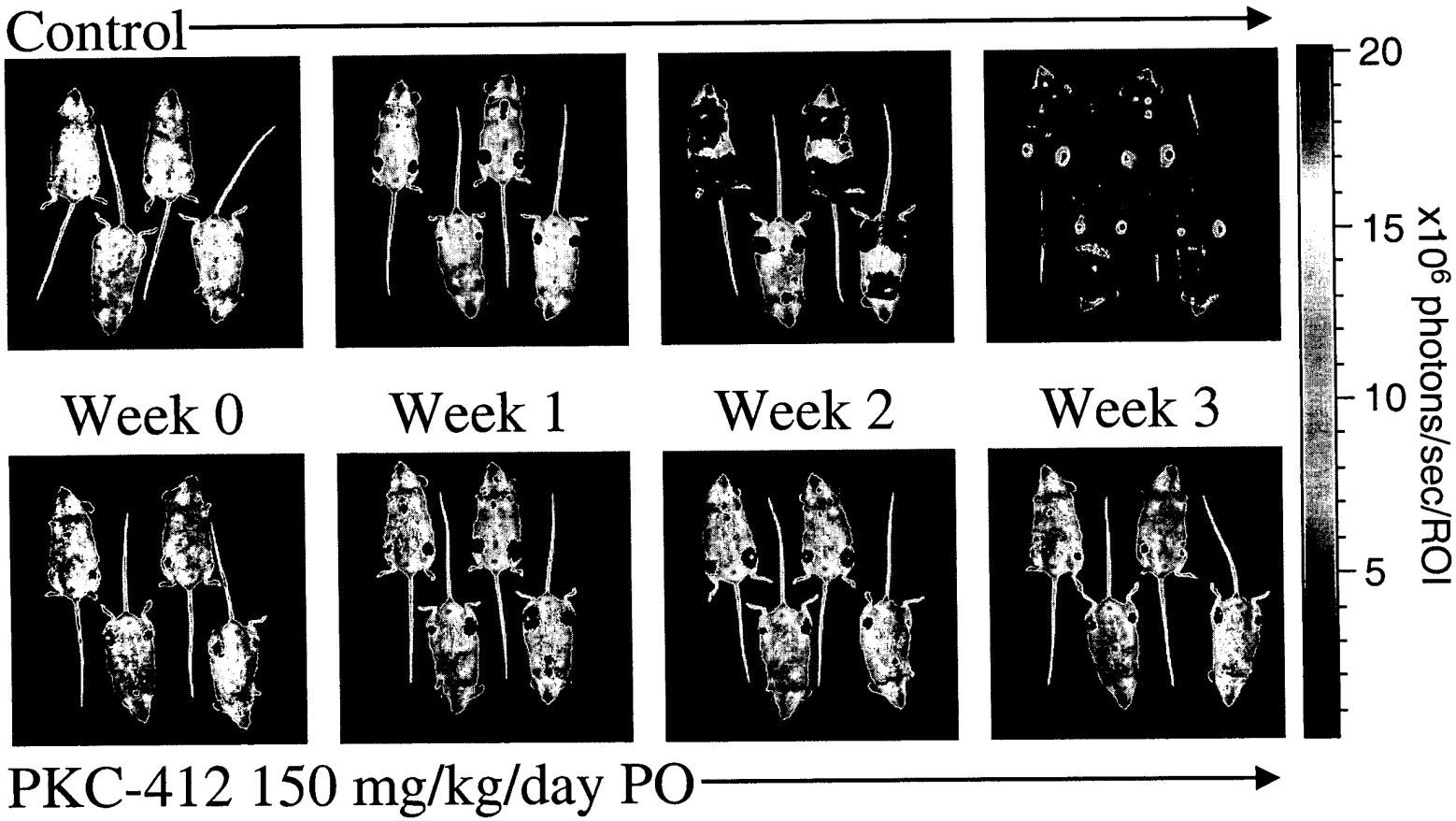


FIG. 15

MLL Leukemia Treated with FLT3 Inhibitor PKC-412

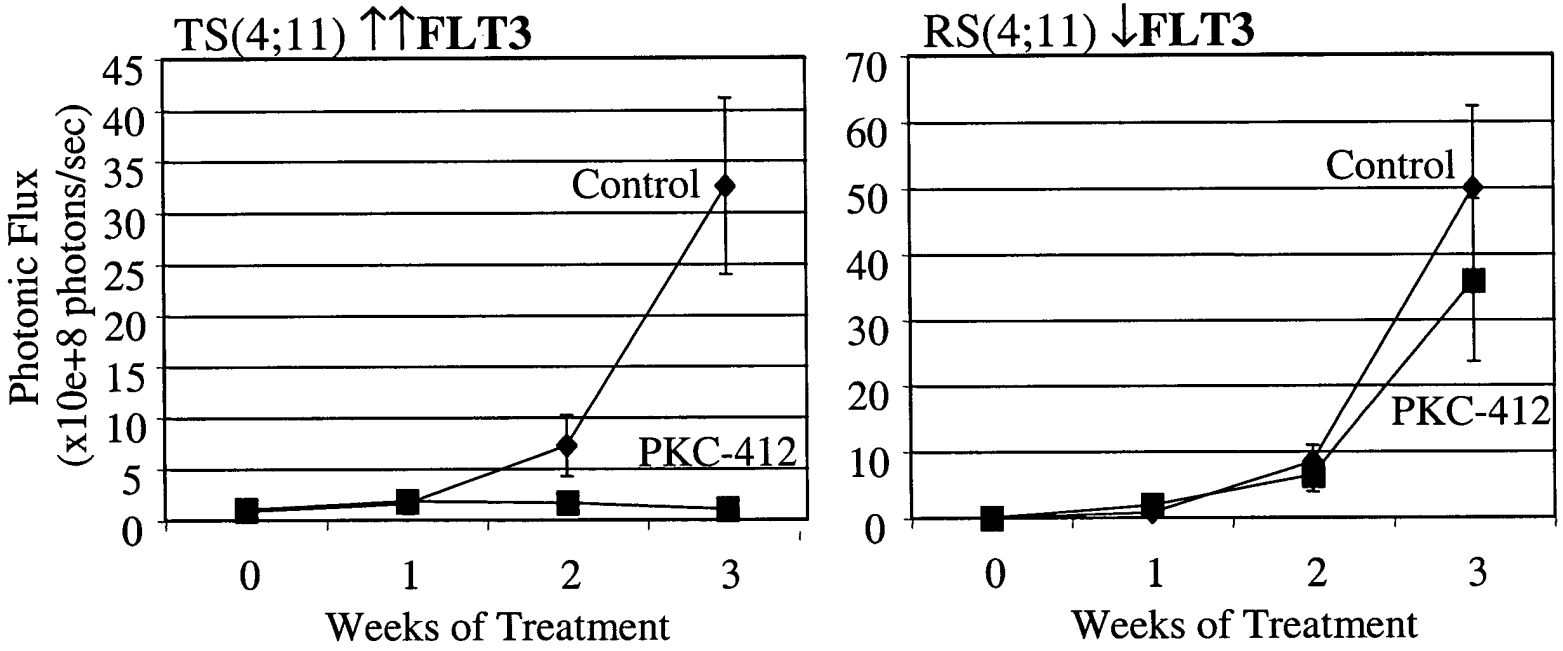
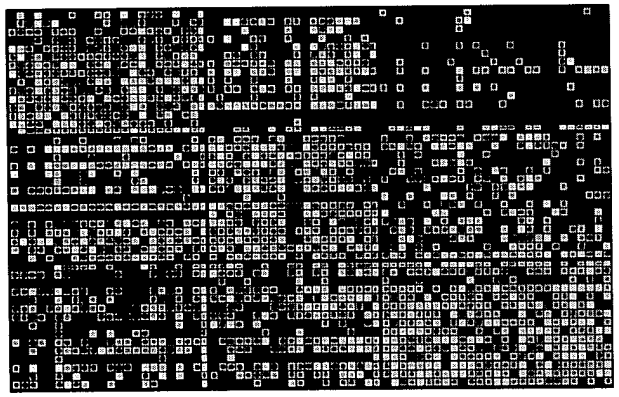


FIG. 16

Validation of FLT3 as a Target in MLL



Retro-shRNA

(?Weeks)

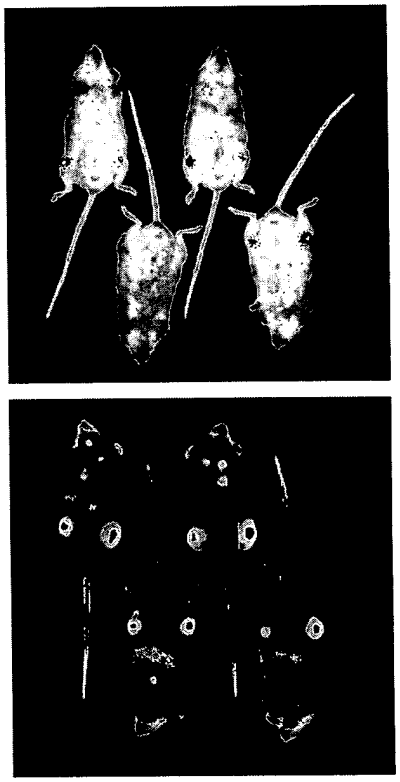
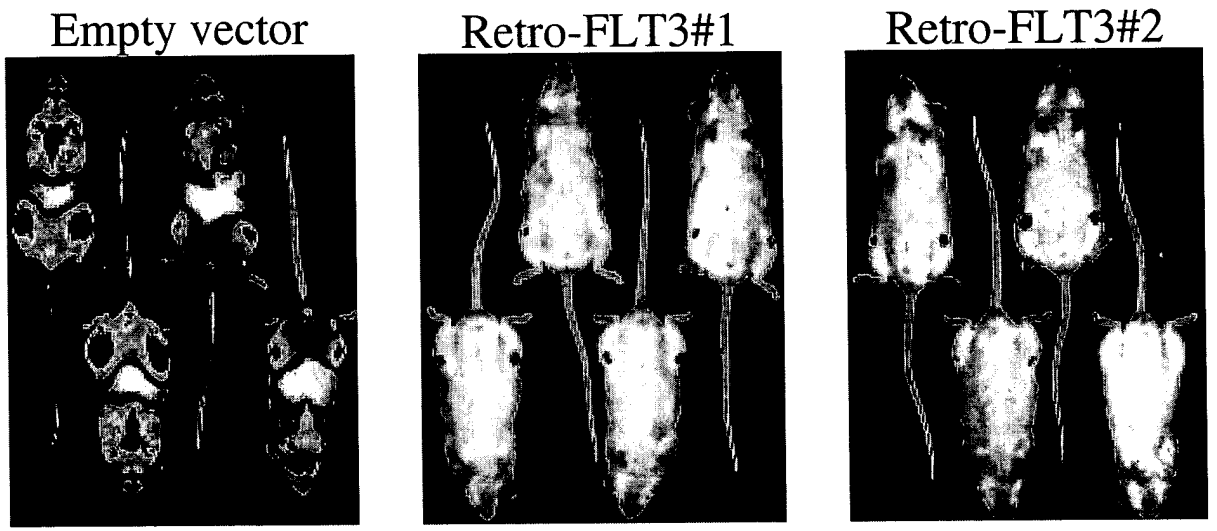


FIG. 17

Validation of FLT3 as a Target in MLL Utilizing shRNA and *In Vivo* Imaging



TS(4;11) cells infected with retrovirus encoding shRNA against FLT3 or empty vector. Selected 4 days with puromycin. 10^6 live cells injected into irradiated NOD-SCID mice. Imaged 10 days after injection.

FIG. 18

ADW Effects in an Orthotopic Model of Multiple Myeloma (MM1S)

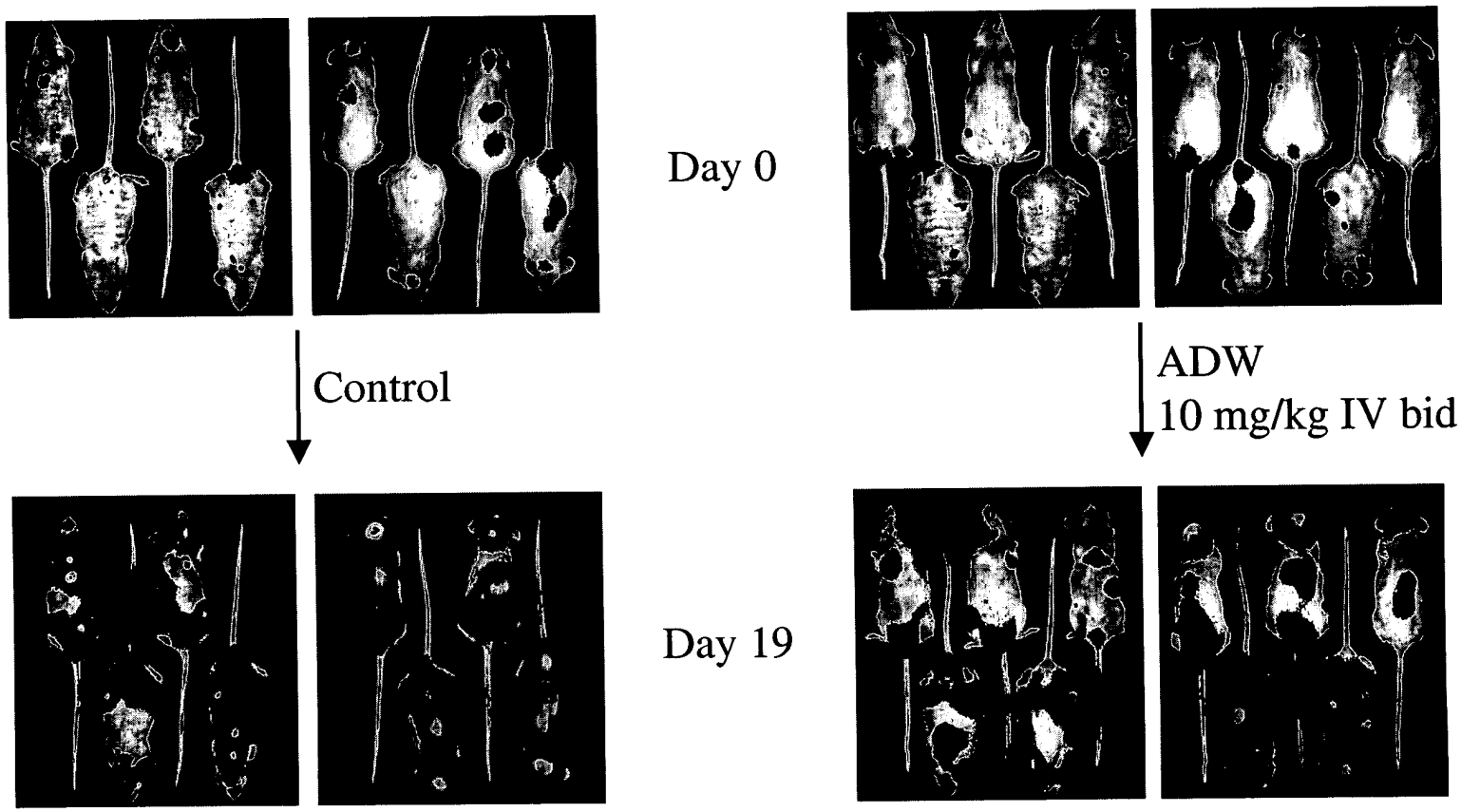
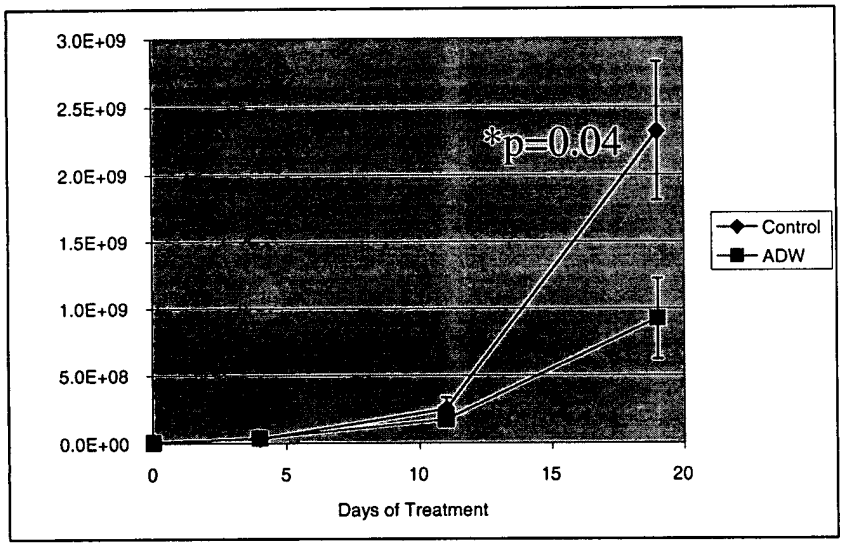


FIG. 19

ADW Effects in an Orthotopic Model of Multiple Myeloma



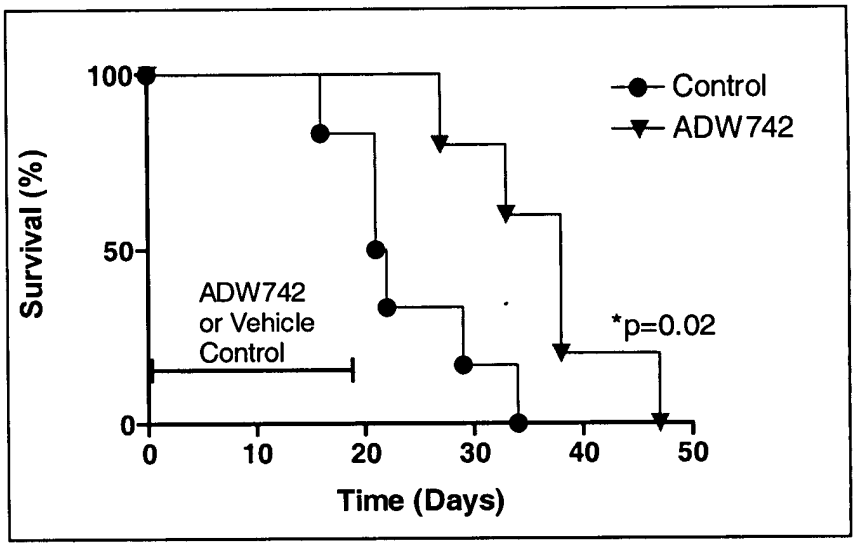


FIG. 20

Efficacy of AMN107 Against 32D/p210-Luc Cells *In Vivo*

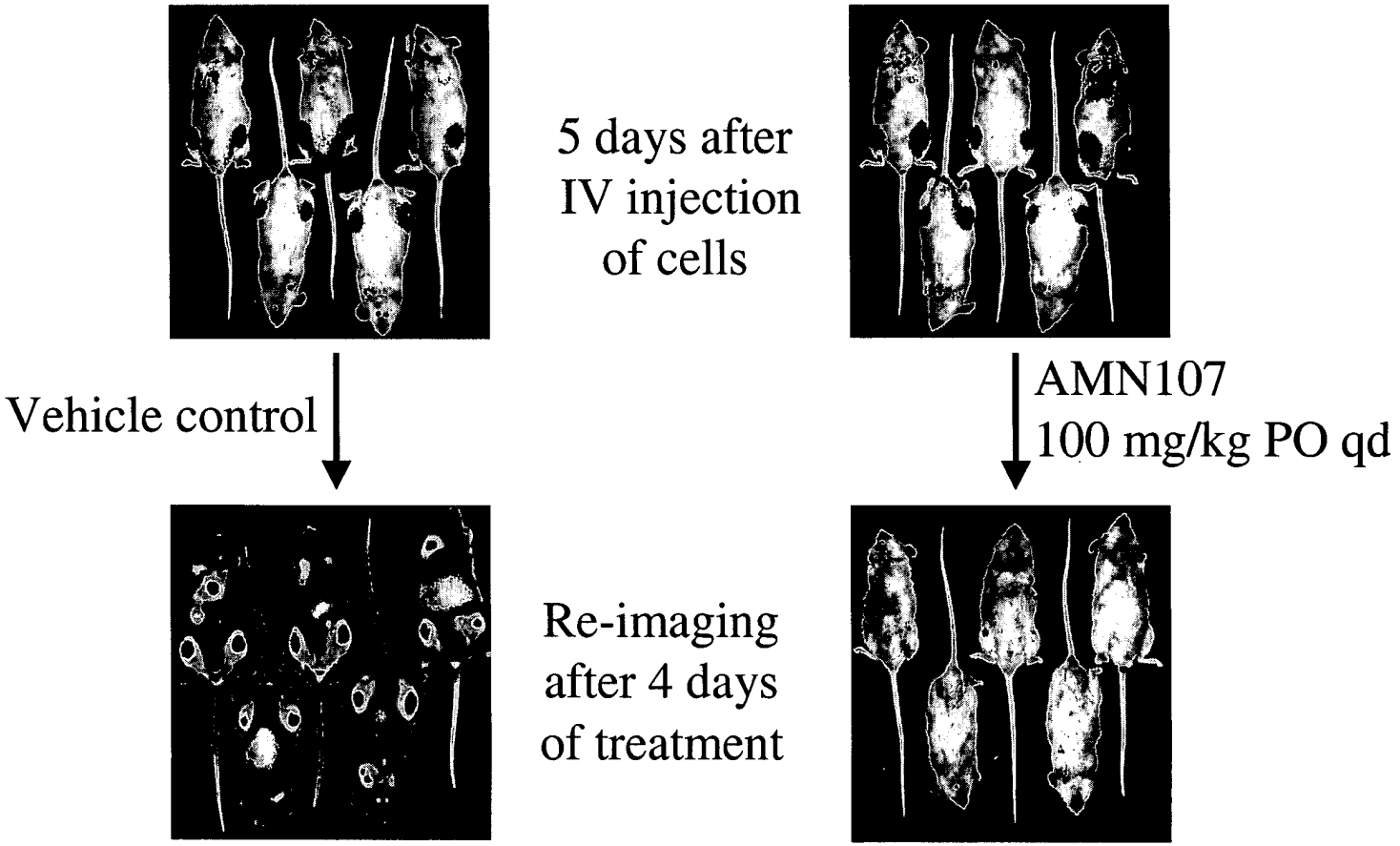
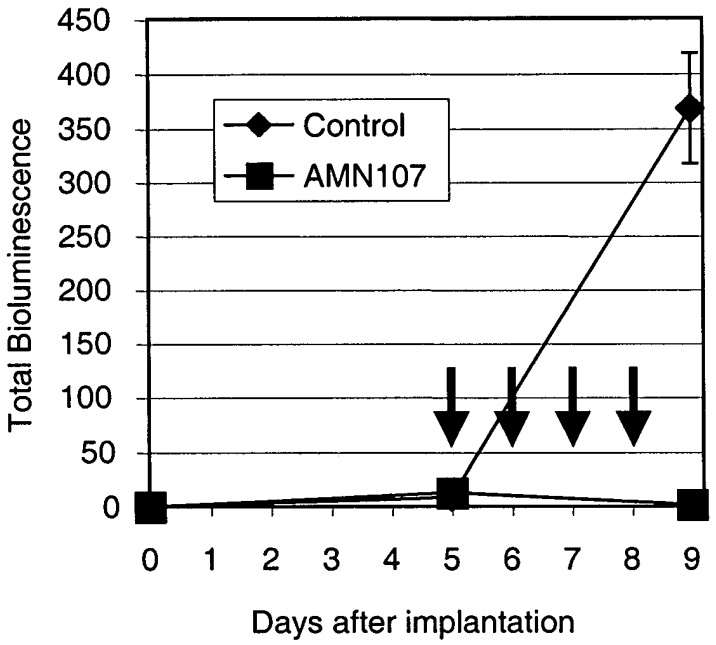


FIG. 21

Quantitation of AMN107 Effects Against 32D/p210-Luc Cells *In Vivo*



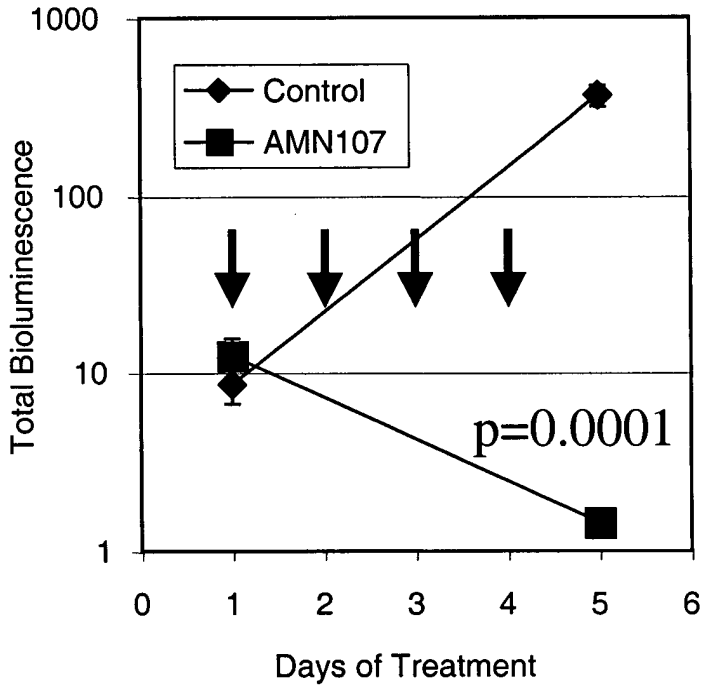


FIG. 22

Orthotopic Brain Tumor Model

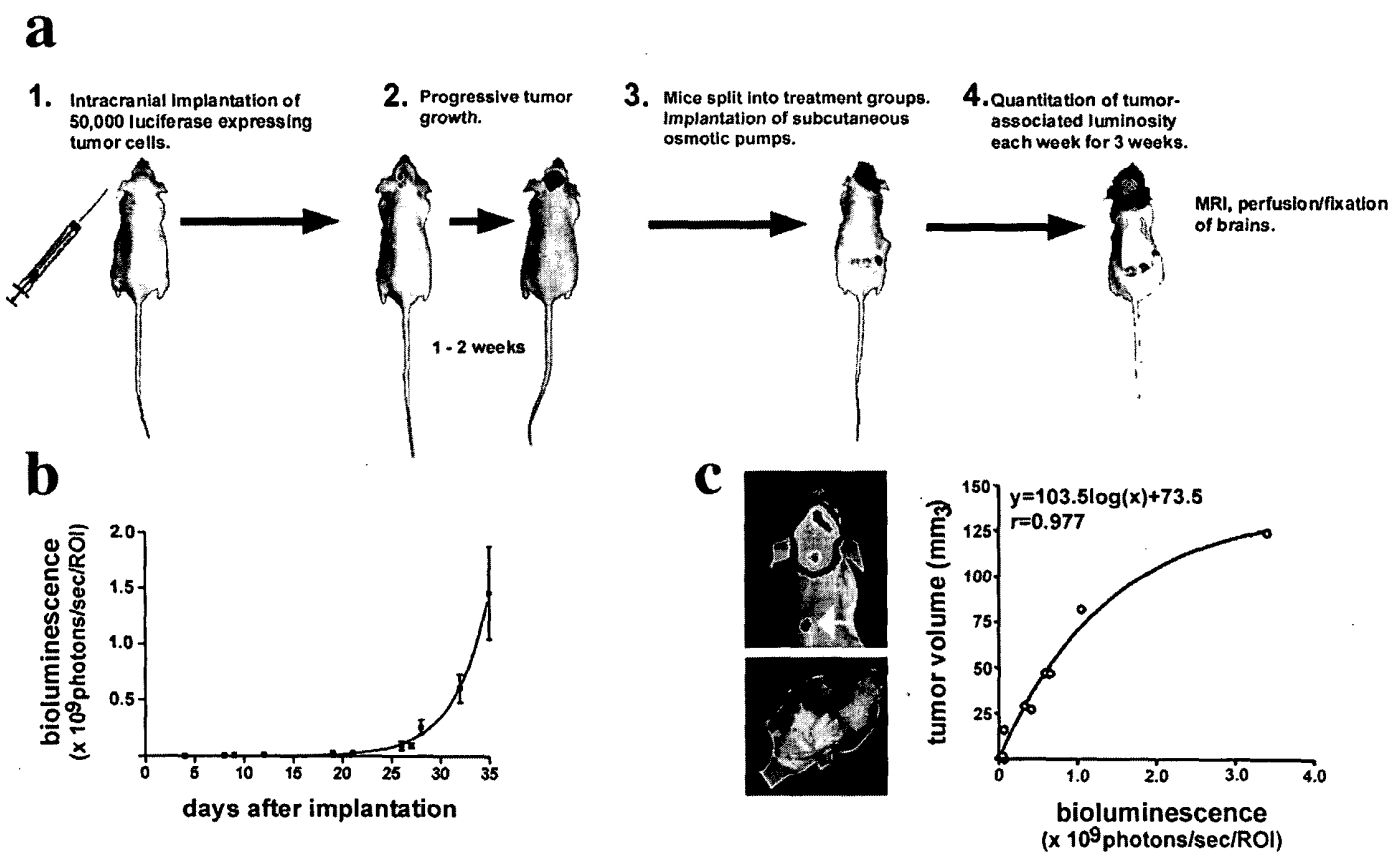


FIG. 23

In Vivo Efficacy of AMD-3100

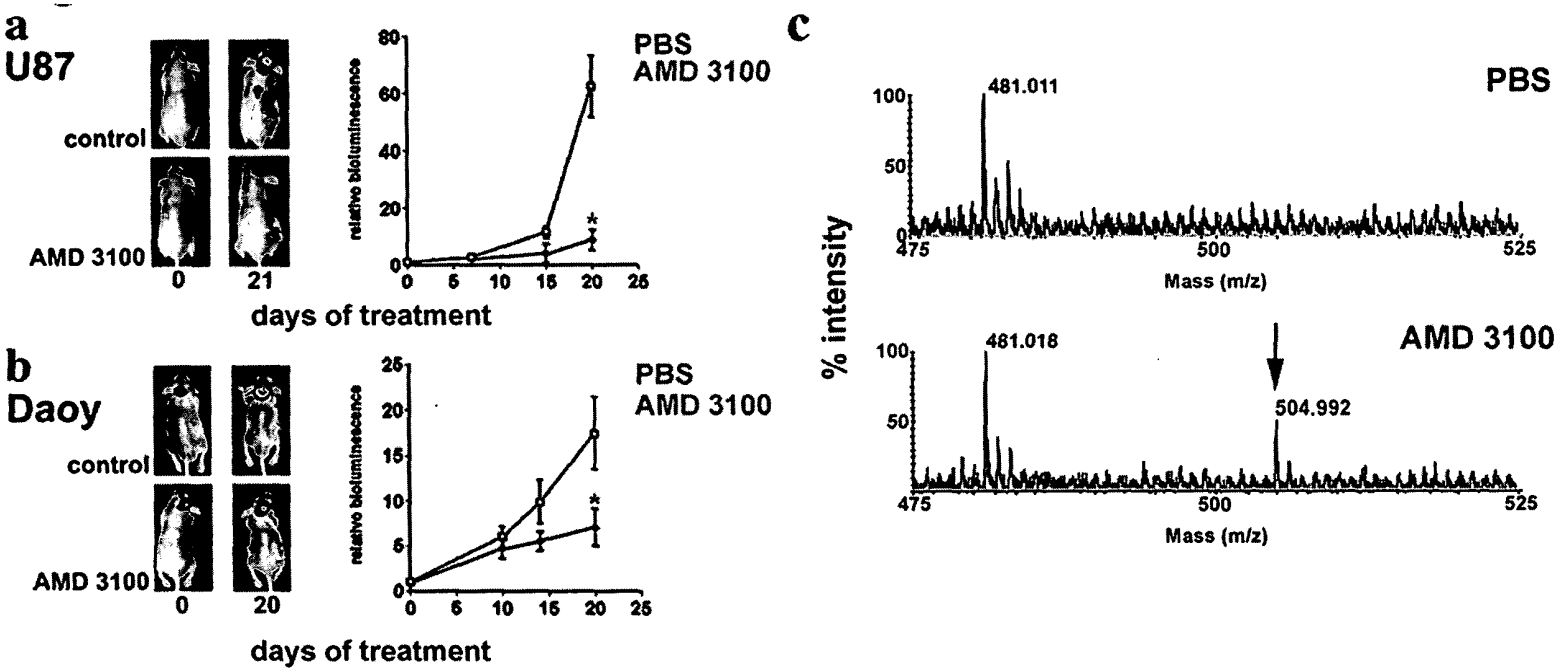


FIG. 24

In Vivo Imaging of Transcriptional Pathway Activity

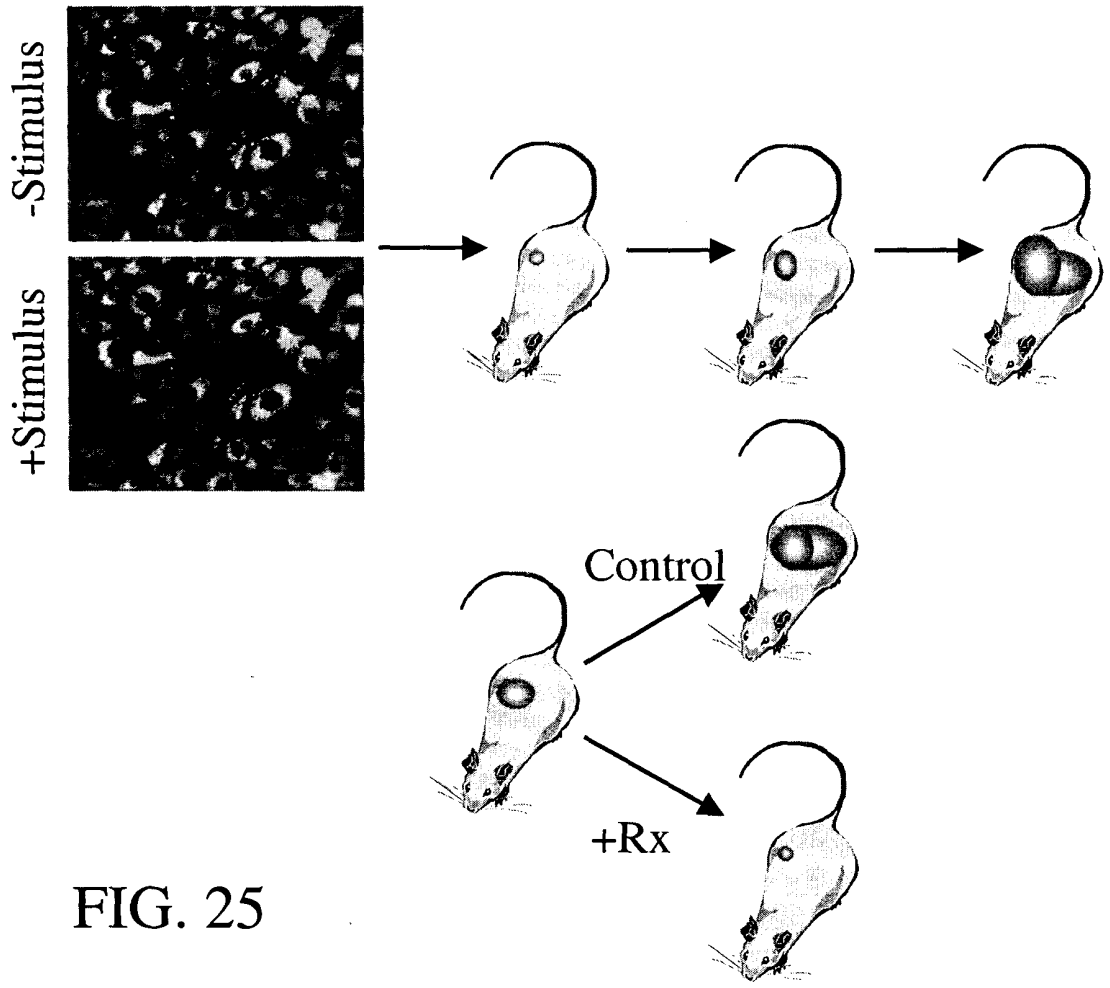


FIG. 25

CXCR4 Inhibition with AMD3100 Attenuates ERK1/2 Signalling *In Vivo*

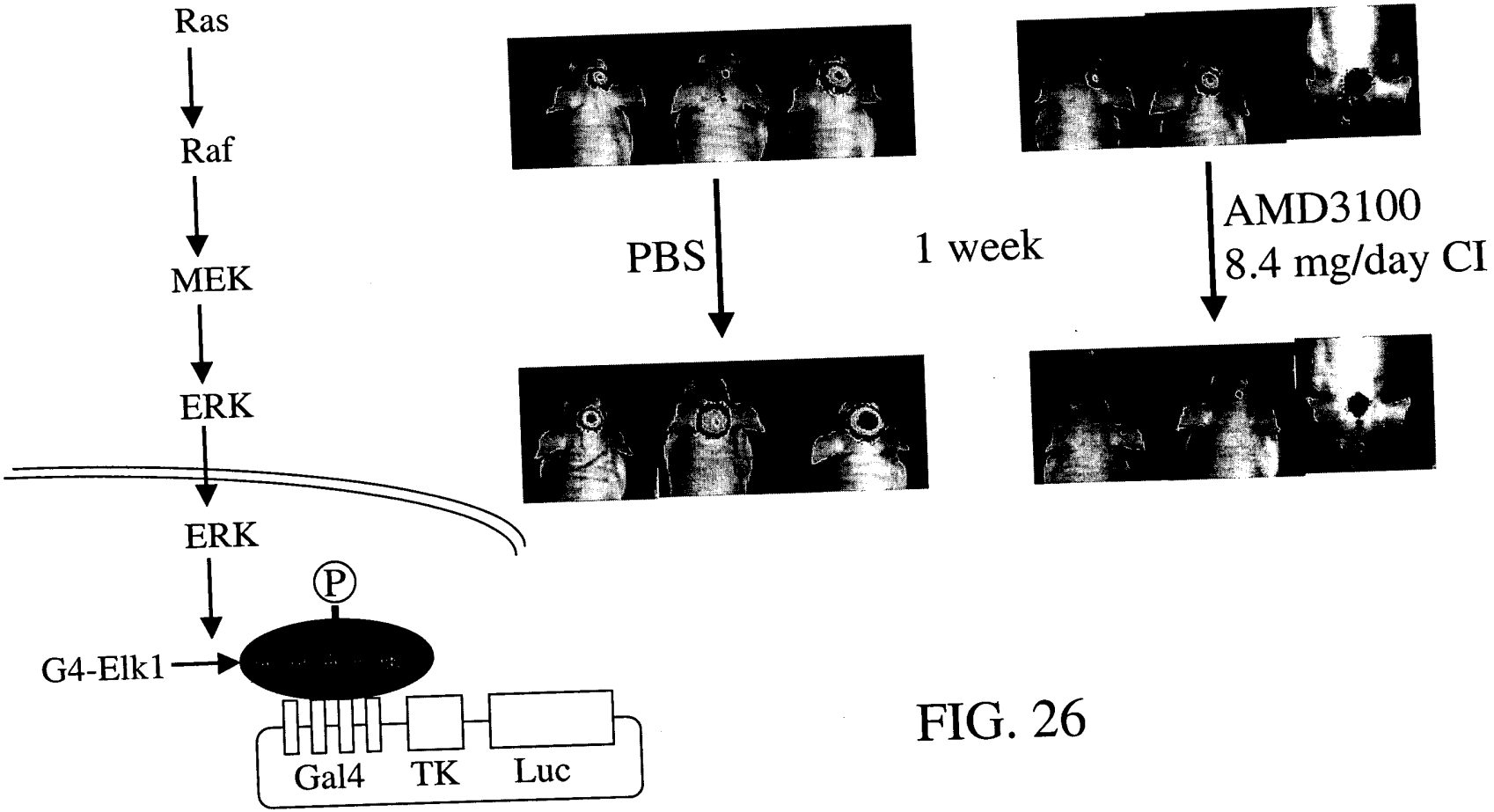


FIG. 26

In Vivo Imaging of Hypoxia-Inducible Reporter Activity

Cell line: HepG2 Epo-Luc c.1
Innoculum: 3 million cells
Time: 48 hrs after implantation

FIG. 27